REMARKS

Claims 6 - 13 and 16 – 17 have been canceled without prejudice. Claims 1, 2, 4, 5, 14, 15 has been amended. Claim 3 was previously presented. Claims 1 – 5, 14 and 15 are pending and are the subject of this Office Action. Support for claims 1 – 5, 14 and 15 can be found throughout the specification including the Drawings and claims as filed originally. No new matter has been added.

Applicants respectfully reserve the right to pursue any non-elected, withdrawn, canceled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

It is submitted that the claims, herewith and as originally presented were in full compliance with the requirements of 35 U.S.C. § 112. The amendment of the claims, as presented herein, is not made for purposes of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, this amendment is made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendment should not give rise to any estoppel.

Reconsideration and withdrawal of the rejections of this application in view of the amendments and remarks herewith, is respectfully requested, as the application is in condition for allowance.

Applicant now turns to comments made by the Examiner in this Office Action as follows.

1. Claim 16 is rejected under 35 U.S.C. §101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

> The Examiner states, "A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world"

context of use for the claimed invention which does not require further research.

Claim 16 is drawn to a method for the prophylaxis and/or treatment of a disease in a mammal, wherein an increased blood concentration and/or a prolonged blood half-life of an endogenous ligand and/or is effective for the prophylaxis and/or treatment of the disease, comprising administering to the mammal an effective amount of an antibody that has an affinity to the endogenous ligand but does not neutralize the same substantially, so as to increase the blood stability of the endogenous ligand, thereby enhancing a receptor activity-regulatory action. The determination of the utility of the claimed invention is limited to the method of treatment of a disease. Since the method does not specify a specific disease, the claimed method does not have a specific and substantial utility.

Claim 16 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim 16 has been canceled thereby obviating the basis for rejection under 35 USC § 101 and 35 U.S.C. §112, first paragraph.

2. Claims 2 and 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner states, "Claims 2 and 16 are indefinite because they recite "a receptor activity-regulatory action". It is unclear what the metes and bounds of the limitation are.

Claims 14 and 16 use the ambiguous language "and/or", rendering the claims indefinite. In addition, the claim language of claim 14 is so ambiguous that the claim fails to particularly point out and distinctly claim the subject matter. Claim 15 is rejected as a dependent claim from claim 14."

Applicants have amended claims 2, 14 and 15 by limiting the "endogenous ligand" to "GLP-1" and limiting "disease" to "metabolic disease". Furthermore, Applicants have amended claim 2 by deleting the phrase "receptor activity-regulatory action thereof" to "the activity of the GLP-1 receptor". Applicants believe these amendments remove any indefiniteness or ambiguity of the claims. In addition, Applicants have canceled claim 16 thereby obviating any basis for rejection of that claim.

3. Claims 1-7, 14, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Frincke et al. (US Patent No. 5,055,289, Oct. 8, 1991).

> The Examiner states, "Frincke et al. teach a method for treating viral diseases and tumors in an animal comprising administering to the animal an effective amount of an endogenous ligand, interferon, and an antibody that binds the interferon at a site which does not substantially impair its therapeutic activity and which extends the serum half-life of the interferon (see, e.g., claim 11). Frincke et al. teach that interferon has a therapeutic effect in the treatment of certain malignant tumors including breast cancer (column 4, lines 8-12). Binding of the antibody to the interferon did not inhibit the antiviral property (column 4, lines 66-68) or anti-proliferative activity (column 5, lines 5-7) of the interferon.
>
> Frincke et al. teach that when alpha-interferon:1FG252.2 complex administered to rats, the serum half-life of interferon was twelve times longer than when alpha-interferon was administered alone, 84 minutes versus 6.8 minutes (column 5, lines 29-47). The blood concentration of the interferon when alpha-interferon:1FG252.2 complex was administered was about seven times higher than when alpha-interferon was administered alone (50,000 u/ml x min versus 7,047 u/m1 x min; column 5, lines 38 and 46).
>
> Thus, the reference of Frincke et al. meets the limitations of claims 1-7, 14, and 15."

Claims 1-7, 10, 14, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Hamaguchi et al. (WO 91/12022, August 22, 1991), as evidenced by Frincke et al. (WO 85/00974, March 14, 1985).

The Examiner further states, "Hamaguchi et al. teach a method for improving the blood stability of IL-2 in rat comprising administering intravenously to the rat an effective amount (a dose equivalent to 100 pig of the rhIL-2) of an immune complex of anti-IL-2 monoclonal antibody and IL-2 (Experimental Example 1, page 39). The serum rhIL-2 concentration was about 7 times higher than when rhIL-2 was administered with a control antibody (page 39, line 20-22). The specific activity of the immune complex per rhIL-2 was identical to that of rhIL-2 itself (page 36, line 3-7). The blood half-life is far less that one week (Fig. 3). Hamaguchi et al. also teach that administering the immune complex of anti-IL-2 monoclonal antibody and IL-2 enhanced anti-tumor effects in mice (Experimental Example 4).

Hamaguchi et al. teach various immune complexes of an antibody (bottom of page 14 to top of page 15) and a cytokine, such as interferon (page 10, line 19) or a hormone, such as calcitonin (page 11, line 17). Hamaguchi et al. further teach that such an immune complex can be used to treat various diseases such as cancer or hormone control abnormality (page 3, 1st paragraph; bottom of page 27 to the 2nd paragraph of page 30).

Hamaguchi et al. further teach an immune complex of a monoclonal antibody and a-interferon prolonged the blood half-life (bottom of page 5 to top of page 6) by twelve times as evidenced by Frincke et al. (WO 85/00974, column 5, lines 29-47).

Thus, the reference of Hamaguchi et al. meets the limitations of claims 1-7, 10, 14, and 15.'.

Applicants wish to address both 102(b) rejections with a collective argument. The Examiner contends that claims 1-7, 10 and 14-16 are not novel, because (1) Frincke et al. (US 5,055,289) teaches a method for treating a viral disease and cancer by co-administration of interferon (IFN) and an anti-IFN antibody, and (2) Hamaguchi et al. teaches the improvement of blood stability of interleukin-2 (IL-2) and the treatment of cancer and abnormal hormone control by administration of a complex of IL-2 and an anti-IL-2 antibody (further disclosing a conjugate of the complex with calcitonin).

Applicants have amended the claims to be limited from "endogenous ligand" to "endogenous GLP-1 produced in a mammalian body" in claim 1. Therefore, Frincke et al. and Hamaguchi et al. cannot be used as anticipatory references. They both teach the exogenous administration of a therapeutic agent which are also different from GLP-1.

In addition, Applicants have inserted the phrase "without administration of GLP-1 from outside the body" into claim 1. The focus of the present invention rests in the enhancement of therapeutic activity of an endogenous ligand inherently present in a patient via the improvement of its blood stability by solely administering an antibody against the ligand to the patient without co-administration of the ligand. Since the therapeutic methods disclosed in Frincke et al. and Hamaguchi et al. requires co-administration of a ligand and an antibody against the ligand, it would not have been obvious to one of skill in the art that a small amount of the endogenous ligand present in a patient body can exert a sufficient therapeutic activity when the ligand is stabilized by an antibody against the same.

Furthermore, the antibody drug of the present invention is also advantageous in that it can exert a therapeutic effect in a smaller amount compared to conventional antibody drugs, and that it does not cause a rapid increase in the blood level.

4. Claims 1-7, 10, and 14-16 are objected to because of the following informalities:

The Examiner states:

(i) Claim 1 has a typographic error in line 1: "An method" should be amended as "A method".

(ii) Claim 7 is incomplete.

(iii). Claim 1-6, 10, and 14-16 recite non-elected endogenous ligands, whereas claims 14-16 are objected to because they recite non-elected diseases.

Appropriate correction is required.

Applicants have amended the claims to address the appropriate corrections.

CONCLUSION

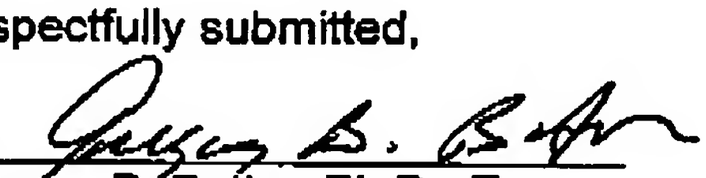
Applicants submit that all claims are allowable as amended and respectfully request early favorable action by the Examiner. Applicant's representative would like to discuss this case with the Examiner to learn if any outstanding issues remain after consideration of this Amendment. If the Examiner believes that a telephone conversation with Applicants' attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

FEE AUTHORIZATION

The Commissioner is authorized to charge the extension fee and any other fees associated with this submission to our Deposit Account No. 04-1105, Reference 66368(46590). Any overpayment should be credited to said deposit account.

Dated: April 21, 2009

Respectfully submitted,

By 

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